

L4 72955 PLASMID OR VECTOR

=> s l3 and l4

L5 63 L3 AND L4

=> s promoter or promoters

27962 PROMOTER

22160 PROMOTERS

L6 36145 PROMOTER OR PROMOTERS

=> s l5 and l6

L7 61 L5 AND L6

=> s marker

L8 36321 MARKER

=> s l7 and l8

L9 52 L7 AND L8

=> d l-52

1. 5,929,307, Jul. 27, 1999, Method for the production of hybrid plants; Thomas K. Hodges, et al., 800/303; 435/320.1, 419, 468; 536/23.6, 23.72, 23.74, 24.1; 800/274, 278, 287, 288, 298 [IMAGE AVAILABLE]

2. 5,929,301, Jul. 27, 1999, Nucleic acid sequence encoding FLP **recombinase**; Christopher L. Baszcynski, et al., 800/278; 435/419; 536/23.1 [IMAGE AVAILABLE]

3. 5,928,914, Jul. 27, 1999, Methods and compositions for transforming cells; Philippe Leboulch, et al., 435/69.1, 70.1, 183, 320.1; 536/23.1 [IMAGE AVAILABLE]

4. 5,925,808, Jul. 20, 1999, Control of plant gene expression; Melvin John Oliver, et al., 800/298; 435/320.1, 419, 468, 469, 470; 536/23.6, 24.1, 24.5; 800/295 [IMAGE AVAILABLE]

5. 5,922,927, Jul. 13, 1999, Methods for producing tetracycline-regulated transgenic mice; Hermann Bujard, et al., 800/25; 435/69.1, 320.1, 325, 455, 463; 800/18, 22 [IMAGE AVAILABLE]

6. 5,912,411, Jun. 15, 1999, Mice transgenic for a tetracycline-inducible transcriptional activator; Hermann Bujard, et al., 435/69.1, 70.1, 325; 536/23.4, 24.1 [IMAGE AVAILABLE]

7. 5,910,415, Jun. 8, 1999, Controlled modification of eukaryotic genomes; Thomas K. Hodges, et al., 435/6, 320.1, 410; 536/23.1 [IMAGE AVAILABLE]

8. 5,888,981, Mar. 30, 1999, Methods for regulating gene expression; Hermann Bujard, et al., 514/44; 424/93.21; 435/455, 463, 465 [IMAGE AVAILABLE]

9. 5,888,732, Mar. 30, 1999, Recombinational cloning using engineered recombination sites; James L. Hartley, et al., 435/6, 91.42, 320.1; 536/23.1, 24.2 [IMAGE AVAILABLE]

10. 5,885,779, Mar. 23, 1999, Repressed trans-activator system for characterization of protein-protein interactions; Ivan Sadowski, et al., 435/6, 69.7, 91.41, 254.2, 320.1, 325; 530/350; 536/23.4, 23.5, 23.7, 24.33 [IMAGE AVAILABLE]

11. 5,882,888, Mar. 16, 1999, DNA integration by transposition; Steen Troels J. o slashed. rgensen, 435/69.1, 91.4, 243, 252.31, 320.1, 473, 477, 478, 489; 536/23.1, 24.2 [IMAGE AVAILABLE]

12. 5,877,400, Mar. 2, 1999, Transgenic methods and compositions for producing parthenocarpic fruits and vegetables; Dwight T. Ternes, et al., 800/260; 435/69.1, 320.1; 536/23.6, 23.7, 24.1; 800/287, 298, 309, 317.1, 317.4 [IMAGE AVAILABLE]

13. 5,871,907, Feb. 16, 1999, Methods for producing members of specific binding pairs; Gregory Paul Winter, et al., 435/6, 69.1, 91.1, 235.1, 320.1, 471, 472, 476, 488 [IMAGE AVAILABLE]

14. 5,866,755, Feb. 2, 1999, Animals transgenic for a tetracycline-regulated transcriptional inhibitor; Hermann Bujard, et al., 800/9, 18 [IMAGE AVAILABLE]

15. 5,859,310, Jan. 12, 1999, Mice transgenic for a tetracycline-

controlled transcriptional activator; Hermann Bujard, et al., 800/9; 435/69.1, 70.1, 320.1, 325; 514/152; 536/23.4, 24.1; 800/4, 18, 22, 25 [IMAGE AVAILABLE]

16. 5,858,657, Jan. 12, 1999, Methods for producing members of specific binding pairs; Gregory Paul Winter, et al., 435/6, 69.6, 91.1 [IMAGE AVAILABLE]

17. 5,851,808, Dec. 22, 1998, Rapid subcloning using site-specific recombination; Stephen J. Elledge, et al., 435/91.4, 91.41, 320.1; 536/23.1 [IMAGE AVAILABLE]

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19. 5,849,572, Dec. 15, 1998, HSV-1 **vector** containing a lat **promoter**; Joseph C. Glorioso, et al., 435/320.1, 235.1; 536/24.1 [IMAGE AVAILABLE]

20. 5,849,571, Dec. 15, 1998, Latency active herpes virus **promoters** and their use; Joseph C. Glorioso, et al., 435/320.1, 456 [IMAGE AVAILABLE]

21. 5,843,744, Dec. 1, 1998, Bacillus thuringiensis Tn5401 proteins; James A. Baum, 435/183, 196 [IMAGE AVAILABLE]

22. 5,840,540, Nov. 24, 1998, Nucleic acids encoding presenilin II; Peter H. St. George-Hyslop, et al., 435/69.1, 252.3, 320.1, 325; 530/350; 536/23.1, 24.3 [IMAGE AVAILABLE]

23. 5,830,698, Nov. 3, 1998, Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same; Mitchell E. Reff, et al., 435/69.1, 320.1, 463, 465; 536/23.2 [IMAGE AVAILABLE]

24. 5,830,461, Nov. 3, 1998, Methods for promoting wound healing and treating transplant-associated vasculopathy; Timothy R. Billiar, et al., 424/94.4, 94.1; 435/189 [IMAGE AVAILABLE]

25. 5,817,492, Oct. 6, 1998, Recombinant DNA viral **vector** for transfecting animal cells; Izumu Saito, et al., 435/456; 424/93.21; 435/320.1, 465; 514/44 [IMAGE AVAILABLE]

26. 5,814,618, Sep. 29, 1998, Methods for regulating gene expression; Hermann Bujard, et al., 514/44; 424/93.21 [IMAGE AVAILABLE]

27. 5,801,030, Sep. 1, 1998, Methods and vectors for site-specific recombination; Duncan L. McVey, et al., 435/456, 320.1, 462; 536/23.1, 23.2 [IMAGE AVAILABLE]

28. 5,789,156, Aug. 4, 1998, Tetracycline-regulated transcriptional inhibitors; Hermann Bujard, et al., 435/6, 69.1, 69.7, 252.3, 320.1, 810; 536/23.4, 23.7, 24.1 [IMAGE AVAILABLE]

29. 5,776,449, Jul. 7, 1998, Recombinant bacillus thuringiensis strains, insecticidal compositions and method of use; James A. Baum, 424/93.2, 93.461, 405; 435/170, 252.31, 832 [IMAGE AVAILABLE]

30. 5,773,697, Jun. 30, 1998, Genetic constructs and methods for producing fruits with very little or diminished seed; Dwight T. Tormes, et al., 800/260; 435/69.1, 320.1; 536/23.7, 24.1; 800/268, 287, 290, 298, 308, 309 [IMAGE AVAILABLE]

31. 5,767,376, Jun. 16, 1998, Nucleic acids encoding a papaya ACC synthase gene; John I. Stiles, et al., 800/298; 435/320.1, 419; 536/23.6; 800/283 [IMAGE AVAILABLE]

32. 5,744,336, Apr. 28, 1998, DNA constructs for controlled transformation of eukaryotic cells; Thomas K. Hodges, et al., 435/320.1; 536/23.1, 24.1, 24.2 [IMAGE AVAILABLE]

33. 5,733,743, Mar. 31, 1998, Methods for producing members of specific binding pairs; Kevin Stuart Johnson, et al., 435/69.1, 252.33, 320.1, 462, 472; 530/387.1 [IMAGE AVAILABLE]

34. 5,723,765, Mar. 3, 1998, Control of plant gene expression; Melvin John Oliver, et al., 800/268; 435/320.1, 418, 419; 536/23.6, 24.1, 24.5; 800/287, 288, 314 [IMAGE AVAILABLE]

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37. 5,679,523, Oct. 21, 1997, Method for concurrent disruption of expression of multiple alleles of mammalian genes; Limin Li, et al., 435/6, 320.1, 463; 536/23.2, 24.5 [IMAGE AVAILABLE]
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39. 5,654,168, Aug. 5, 1997, Tetracycline-inducible transcriptional activator and tetracycline-regulated transcription units; Hermann Bujard, et al., 435/69.1, 320.1; 536/23.7, 24.1 [IMAGE AVAILABLE]
40. 5,650,308, Jul. 22, 1997, Recombinant *Bacillus thuringiensis* strain construction method; James A. Baum, 435/485, 252.31, 320.1 [IMAGE AVAILABLE]
41. 5,650,298, Jul. 22, 1997, Tight control of gene expression in eucaryotic cells by tetracycline-responsive **promoters**; Hermann Bujard, et al., 435/69.7, 320.1, 463; 536/23.4, 24.1 [IMAGE AVAILABLE]
42. 5,635,381, Jun. 3, 1997, Agrobacterium bacteria capable of site-specific recombination; Paul J. J. Hooykaas, et al., 800/294; 435/71.2, 199, 252.2, 252.3, 320.1, 419, 477; 536/23.72 [IMAGE AVAILABLE]
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45. 5,530,191, Jun. 25, 1996, Method for producing cytoplasmic male sterility in plants and use thereof in production of hybrid seed; Pal Maliga, 800/274; 47/DIG.1; 800/287, 298, 303 [IMAGE AVAILABLE]
46. 5,527,695, Jun. 18, 1996, Controlled modification of eukaryotic genomes; Thomas K. Hodges, et al., 800/291; 435/320.1 [IMAGE AVAILABLE]
47. 5,510,099, Apr. 23, 1996, Mutagenesis testing using transgenic non-human animals carrying test DNA sequences; Jay M. Short, et al., 800/3; 424/9.1; 435/317.1, 320.1, 488 [IMAGE AVAILABLE]
48. 5,478,731, Dec. 26, 1995, Polycos vectors; Jay M. Short, 435/91.4, 235.1, 252.3, 252.33; 536/23.1 [IMAGE AVAILABLE]
49. 5,441,884, Aug. 15, 1995, *Bacillus thuringiensis* transposon TN5401; James A. Baum, 435/252.31; 424/93.2; 435/252.3, 252.33, 320.1; 536/23.1, 23.2, 23.7, 24.1 [IMAGE AVAILABLE]
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51. 5,378,618, Jan. 3, 1995, Vitro headful packaging system for cloning DNA fragments as large as 95kb; Nat L. Sternberg, et al., 435/91.1, 91.5, 320.1, 472 [IMAGE AVAILABLE]
52. 4,959,317, Sep. 25, 1990, Site-specific recombination of DNA in eukaryotic cells; Brian L. Sauer, 435/462, 69.1, 91.1, 91.41, 254.2, 254.21, 320.1, 477 [IMAGE AVAILABLE]

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US PAT NO: 5,888,732 [IMAGE AVAILABLE] L9: 9 of 52

ABSTRACT:

Recombinational cloning is provided by the use of nucleic acids, vectors and methods, in vitro and in vivo, for moving or exchanging segments of DNA molecules using engineered recombination sites and recombination proteins to provide chimeric DNA molecules that have the desired characteristic(s) and/or DNA segment(s).

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ABSTRACT:

The present invention provides methods for site-specific recombination in a cell, as well as vectors which can be employed in such methods. The methods and vectors of the present invention can be used to obtain persistent gene expression in a cell and to modulate gene expression. One preferred method according to the invention comprises contacting a cell with a **vector** comprising an origin of replication functional in mammalian cells located between first and second recombining sites located in parallel. Another preferred method comprises, in part,

contacting a cell with a **vector** comprising first and second recombining sites in antiparallel orientations such that the **vector** is internalized by the cell. In both methods, the cell is further provided with a site-specific **recombinase** that effects recombination between the first and second recombining sites of the **vector**.

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L1 221 S RECOMBINASE
L2 464 S LOX
L3 64 S L1 AND L2
L4 72955 S PLASMID OR VECTOR
L5 63 S L3 AND L4
L6 36145 S PROMOTER OR PROMOTERS
L7 61 S L5 AND L6
L8 36321 S MARKER
L9 52 S L7 AND L8

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